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08/580,384	05/20/96	STEINEMANN T	D5715D

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EXAMINER	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 19

Application Number: 08/580,384
Filing Date: 5-20-96
Appellant(s): Steinmann et al

Benjamin Adler
For Appellant

EXAMINER'S ANSWER

This is in response to appellant's brief on appeal filed 9-18-00.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

All claims stand or fall together.

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

The following is a listing of the prior art of record relied upon in the rejection of claims under appeal.

(9) Prior Art of Record

The following is a listing of the prior art of record relied upon in the rejection of claims under appeal.

4,240,163	**GALIN**	**12-1980**
5,151,268	**BANG**	**9-1992**
5,147,638	**ESMON**	**9-1992**

Iverson, D.A., "Inhibition of Intraocular Fibrin Formation Following Infusion of Low-Molecular Weight Heparin During Vitrectomy." Arch. Ophthalmol. Vol. 109, (March 1991), pp. 405-409.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

1. Claims 22-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Galin or Iverson in combination with Bang and Esmon.

Galin teaches that the anticoagulant, heparin inhibits blood clotting and inflammation of eye (note the abstract, columns 2-3 and claims). Galin however, does not teach the use of Protein C.

Iverson teaches that the intraocular fibrin formation during vitrectomy is inhibited by heparin (note the abstract and page 405). Iverson does not specifically teach the use of protein C.

Esmon teaches that Tumor necrosis factor (TNF) causes inflammatory changes at the endothelial cells and also stimulates microvascular thrombosis (note column 3, line 65 through col. 4, line 13). Esmon further teaches that activated protein C reduces the production of TNF (col. 4, line 41 et seq.). Esmon also discusses the role of protein S (col. 2, line 45 et seq.).

Bang teaches that protein C enhances the lysis of fibrin. Bang further teaches that the activated protein C is a novel antithrombotic agent with wider therapeutic index than available anticoagulants such as heparin and will be more effective and less likely to cause bleeding complications than heparin (note col. 1, line 23 through col. 2, line 33; col. 18, line 56 et seq., col. 19, line 33 et seq.).

The references of Galin and Iverson clearly show the use of heparin for the inhibition of inflammation of eye and fibrin formation. The reference of Esmon teaches that protein C reduces the amounts of TNF which is responsible for the formation of clots (fibrin), adhesion of PMNs, blood monocytes and subsequent inflammation. The reference of Bang shows the superiority of protein C over heparin. The use of protein C which is known to decrease TNF which is the cause of fibrin formation and the inflammation instead of heparin would have been obvious to an artisan since Bang teaches its superiority.

Applicants' arguments have been fully considered, but are not found to be persuasive.

Applicants argue that Galin and Iverson do not suggest proctein C as an alternative to heparin in the ocular environment. This was recognized by the examiner and and therefore, these references were combined with the references of Bang and Esmon which recognize the use of protein C.

Applicants while recognizing that Bang is suggestive of the effectiveness of protein C in replacing heparin in a wide variety of thrombotic comditions and also its more usefulness than heparin in treating those conditions argue that Bang makes no observations regarding the applicability of protein C to inflammatory condtions. This argument is not found to be persuasive since the reference of Esmon which is used in combination is suggestive of the anti-inflammatory effect of protein C through its inhibitory effect on tumor necrosis factor. Applicants also argue that Bang limits the administration of protein C to parenteral methods. This argument is not pertinent since instant claim 1 does not recite the mode of administration. Furthermore, as recognized by applicants themselves, the purpose in Bang is to ensure its delivery in the blood stream in an effecitve form. It is within the skill of the art to recognize that an 'eye' has blood capillaries and whatever enters the blood stream enters the capillaires of eye also. Furthermore, instant claims recite 'intraocular inflammation' and this term does not exclude the inflammation of the endothelials of the capillaries in the ocular tissue. Therefore, the examiner disagrees with applicants' interpretation of Bang that he fails to

provide a reasonable expectation that protein C would be effective in the ocular environment.

Applicants argue that Esmon does not teach the presence of TNF in the ocular envoironment; applicants further argue that Esmon provides no evidence that the biochemical cascade of events described therein occurs either in either aqueous or vitreous humor of the eye. These arguments are not found to be persuasive for the reason that, as pointed out above, instant claims do not exclude inflammation of the endothelial cells in the blood capillaries and Esmon's discussion of the effect of TNF is at the endothelial cell level (note col. 3, line 65 et seq.). On the same basis, applicants' arguments that ocular environment differs from other tissues in that it is isolated from the blood stream are not persuasive (that is, instant claims do not exclude inflammation of the blood capillaries in ocular tissue).

Applicants' arguments regarding the formation of the thrombin-thrombomodulin complex and the subsequent fibrin formation cascade of reactions are not found to be persuasive since first of all instant claims are drawn to a method of treatment of inflammation and not the pathway leading to the antithrombotic effect. Furthermore, the cascade of chemical reactions and the subsequent fibrin formation is a vascular phenomenon and not dependent on the tissue. Indeed the cascade of reactions argued by applicants is elegantly discussed on col. 1, line 36 through col. 2, line 30. It is clearly evident from these lines that protein C is anti thrombotic irrespective of the tissue in which the

blood vessels are located. In response, applicants argue that ocular environment is different from other tissues in that it is isolated from the blood stream by the blood-aqeuous barrier. This argument is not persuasive since as pointed above, instant claims do not exclude the inflammation in the eye blood capillaries and there is no barrier within the capillaries themselves.

2. Claims 28-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Galin or Iverson in combination with Bang and Esmon as applied to claims 22-27 above, and further in view of Stocker.

The primary references do not teach the use of protein S in addition.

Stocker while disclosing the use of protein C activators teaches that protein S potentiates the action of protein C (note the abstract, column 1, lines 16-19).

The use of protein S in addition, would have been obvious to one of ordinary skill in the art because of the potentiating effect taught by Stocker.

Applicants' arguments with regard to the primary references have been addressed by the examiner above. Applicants while agreeing that Stocker might be indicative of potentiation of protein C activity by protein S, argue that Stocker provides no information on the activity of either protein C or protein S in the ocular environment. This argument is not found to be persuasive since as pointed out above, instant claims do not exclude inflammation of the blood capillaries in the eye and hence though Stoker does not specifically teach ocular tissue, his teachings are still applicable.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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GSK
January 29, 2001

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